REMARKS

Claims 18-21 and 23-26 are pending. Claims 18-26 are rejected. Reconsideration and withdrawal of the rejections set forth in the Office Action dated March 19, 2004 are respectfully requested.

I. Amendments

Claim 18 is amended to include the dosage feature of claim 22. The dosage is specified as being a daily dose of between 10^8 – 10^{10} Units. Support for recitation of a daily dose is found in the specification at least in the paragraph bridging pages 4 and 5, wherein various embodiments are set forth, each specifying a dosage of ovine interferon-tau between about 10^8 – 10^9 Units/day. Further support for this amendment may be found on page 12, lines 27-29 of the specification, wherein Applicants state that the dosage of interferon-tau will typically be between about $1x10^5$ and 10^{10} Units/day, preferably between about $1x10^8$ and $1.5x10^9$ Units/day.

Claim 19 is amended to correct an improper antecedent basis reference.

No new matter has been added by these amendments.

II. Obvious-type double patenting rejection

Claim 21 was provisionally rejected under the judicially created doctrine of obviousness type double patenting as being unpatentable over claim 8 of co-pending Application No. 10/698,927.

In response, Applicants respectfully request that this rejection be held in abeyance until allowable subject matter is identified in one of the pending cases.

III. Rejections under 35 U.S.C. §112, second paragraph

Claim 22 was rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicant regards as the invention. In particular, the Examiner has asked, "[i]n claim 22, is the intent a one-dose treatment of 10^8 – 10^{10} units, or is the intent actually units per day?" (Office Action mailed March 19, 2004; page 3).

As noted above, the dosage feature of claim 22 is incorporated into claim 18. Claim 18 recites oral administration of interferon-tau at a daily dose of between $10^8 - 10^{10}$ Units. Support for daily administration of the dose is found in the specification at least in the paragraph bridging pages 4 and 5, wherein various embodiments are set forth, each specifying a dosage of ovine interferon-tau between about $10^8 - 10^9$ Units/day. Further support for this amendment may be found in the specification on page 12, lines 27-29, wherein Applicants state that the dosage of interferon-tau will typically be between about $1x10^5$ and 10^{10} Units/day, preferably between about $1x10^8$ and $1.5x10^9$ Units/day.

No new matter has been added by this amendment.

Withdrawal of the rejection under 35 U.S.C. §112, second paragraph is therefore respectfully requested.

IV. Rejections under 35 U.S.C. §112, first paragraph

Claims 18-26 were rejected under 35 U.S.C. §112, first paragraph as allegedly failing to comply with the enablement requirement. Specifically, the Examiner has stated that "...the human clinical trial data presented in the specification do not show any clear pattern relating increased OAS to improvement in the subject's condition," (Office Action mailed March 19, 2004; paragraph bridging pages 3 and 4). Thus, the Examiner is of the mind that the data in the application as filed fails to support the claims; that the data are too scattered. Applicants respectfully traverse this rejection for the following reasons.

A. Analysis

M.P.E.P. 2164.05 states that evidence provided by the applicant in support of enablement "need not be conclusive but merely convincing to one skilled in the art."

Claim 18 (and all claims dependent therefrom) include administering interferon-tau orally to induce OAS levels to treat a viral infection. Specifically, claim 18 recites administering interferon-tau to the subject at a dosage of between $10^8 - 10^{10}$ Units/day, the dose being effective to stimulate bloodstream levels of OAS relative to bloodstream levels of OAS prior to treatment.

Experiments performed in support of the present invention include oral and intraperitoneal administration of interferon-tau to induce OAS activity in a murine model,

as well as oral administration of interferon-tau to induce OAS activity in patients with HCV infections, in human clinical trials. An increase in OAS levels (which in turn results in the degradation of viral mRNA through activation of RNAse), and a decrease in ALT (alanine aminotransferase, which is elevated in persons suffering from chronic hepatitis C infections), is shown throughout Tables 3-6. A general trend shows an increase in OAS coincident with a drop in HCV and ALT over the course of treatment.

For example, patient[1] MSM/00, *see* page 16 of the specification, shows a progressive increase in OAS levels throughout the treatment period. In all but one measurement, OAS levels are higher than the pre-treatment level (11.05 pmol/dL). Patient[2] AMC/007, *see* page 19 of the specification, shows a similar trend. In every case, OAS levels are higher than pre-treatment levels; and in one case (day 29), OAS levels are more than 10-fold higher (120.00 pmol/dL) than the pre-treatment level (11.20 pmol/dL). Here, there is a significant reduction in viral titer levels, coincident with an increase in blood OAS levels, over a treatment period of 2 weeks, at which point treatment is stopped. In addition, patient[2] DBF/012, *see* page 19 of the specification, shows a significant increase in blood OAS levels. In all but three of nine case, OAS levels are higher than pre-treatment levels. At day 71, blood OAS levels had increased by a factor of six (168 pmol/dL versus 28.80 pmol/dL at screen). Overall, Applicants' data support the summary on page 10, lines 32-33 of the specification, wherein it is stated that "[s]everal human patients had 2 to 12 fold increases in their OAS enzyme activity levels as shown in Tables 3-6."

The mouse data depict a statistically significant and dose-dependent relationship between administration of interferon-tau and increased OAS levels, *see*, for example, Figure 1. Bar three shows that OAS levels in mice whole blood following intraperitoneal

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[1]Patient MSM/00 was treated with a total daily dose of 1 mg interferon-tau, which is equivalent to 4.8×10^8 Units/day. *see* page 14, lines 25-26 for the specific antiviral activity of interferon-tau.

[2]Patients AMC/007 and DBF/012 were treated with a total daily dose of 3 mg interferon-tau, which is equivalent to 1.5×10^9 Units/day. *see* page 14, lines 25-26 for the specific antiviral activity of interferon-tau.

or gastric administration of ovine interferon-tau were significantly higher than OAS levels in the control.

The human data, taken together with the mouse data, provide an indication that oral administration of interferon-tau is effective to induce OAS and reduce viral titer in persons infected with HCV.

The first paragraph of 35 U.S.C. §112 requires that the specification of a patent enable any person skilled in the art to which it pertains to make and use the claimed invention without undue experimentation (*e.g.*, *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Applicants submit that this standard is also met by the specification. Specifically, in practicing the methods of the invention, as embodied in claims 18-21 and 23-26, one skilled in the art would have to make or provide for a formulation of interferon-tau as well as a mechanism for measuring blood OAS levels. The specification provides ample guidance for one of skill to make each of these elements.

With respect the use of the interferon-tau as recited in the method of claims 18-21 and 23-26, Example 3 provides an actual reduction to practice of the invention. The data show sufficient predictability to teach one of skill in the art how to use the invention as claimed.

Accordingly, Applicants submit that the specification teaches one of skill in the art how to make and use the invention as presently claimed without undue experimentation as required under 35 U.S.C. §112, first paragraph. Applicants additionally submit that the mouse and human data when considered as a whole support the claim that oral administration of interferon-tau is effective to induce OAS and reduce viral titer in persons infected with HCV. Withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is therefore respectfully requested.

V. Rejection Under 35 U.S.C. §103

Claims 18-23 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Soos *et al.* (U.S. Patent No. 6,372,206). This rejection is respectfully traversed for the following reasons.

A. The Invention

The present invention, as embodied by independent claim 18, is directed to a method for treating HCV in a human subject comprising 1) orally administering interferon-tau to the subject at a daily dosage between 10^8 – 10^{10} Units, the dosage effective to stimulate bloodstream levels of OAS relative to bloodstream levels of OAS prior to treatment, and 2) continuing to orally administer interferon-tau to the subject in such an effective amount until an improvement in the subject's condition is observed.

B. The Prior Art

Soos *et al.* teach that oral administration interferon-tau is effective to treat autoimmune disorders, numerous cell proliferative disorders, and a long list of viral diseases at dosage concentration of between 10^5 – 10^8 Units per day.

Nowhere do Soos, *et al.* teach that oral administration of interferon-tau is effective to stimulate bloodstream levels of OAS. Nor do Soos *et al.* show or suggest the use of high dosage compositions of interferon-tau e.g. between 10^8 – 10^{10} Units/day, to increase blood OAS levels for the treatment of HCV.

C. Analysis

According to M.P.E.P. §2143.03, "[t]o establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). Furthermore, [i]f an independent claim is nonobvious under 35 U.S.C. 103, then any claim dependent therefrom is nonobvious." *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

The present method involves treating HCV in a human subject by orally administering interferon-tau to the subject at a daily dosage between 10^8 – 10^{10} Units, the dosage being effective to stimulate bloodstream levels of OAS relative to bloodstream levels of OAS prior to treatment.

Soos *et al.* describe treating hepatitis C virus with oral interferon-tau, but make no mention of Applicants' requirement that the amount of interferon-tau administered must be

sufficient to raise bloodstream levels of OAS. The feature in Applicants' claimed invention, as recited in independent claim 18, that OAS stimulation must occur, is not shown in Soos *et al.* Nor do Soos *et al.* show or suggest that interferon-tau when administered at a daily dose between $10^8 - 10^{10}$ Units would be effective to raise blood OAS levels. Soos *et al.* do not teach the high dosage composition recited in amended claim 18. Soos *et al.* teach that a preferable dosage is between about $10^6 - 10^7$ Units per day (*see* column 4, line 36).

Since the cited document fails to show or suggest all of the claim limitations, the standard for obviousness has not been met, and withdrawal of the rejection under 35 U.S.C. §103(a) is respectfully requested.

VI. Conclusion

In view of the above amendments and remarks, Applicants submit that the claims now pending are in condition for allowance. A Notice of Allowance is, therefore, respectfully requested.

If in the opinion of the Examiner a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4402.

Respectfully submitted,

Date: June 21, 2004

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